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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/831,629 | 08/17/2001 | Rina Aharoni | AHARONI 5B | 6949 |

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| EXAMINER | |
|---|---|
| LUKTON, DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 02/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/831,629 | AHARONI ET AL. | |
| | Examiner | Art Unit | |
| | David Lukton | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 16-30 and 32-34 remain pending.

The previous species elections remain in force [(a) copolymer-1 having all-L amino acids, (b) an average MW of 7 kD, and (c) net positive charge] , along with the new species elections (HVGD and thyroid tissue).

✧

35 U.S.C §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter or any new and useful improvement therof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 16-30 and 32-34 are rejected under 35 USC §101 because the claimed invention is not supported by a well established utility.

The claims recite that GVDH (and HVGD) can be "prevented". However, there is no evidence that this is the case. The term "prevention" implies that not a single test subject exhibits any symptoms of the disease at all. The "bar" that must be overcome in showing this is quite high. For example, suppose that one of the claimed compounds were administered to each of 10,000 rats. Suppose further that of these 10,000 rats, 9,999 of them failed to develop symptoms of GVDH (or HVGD) as a consequence of being administered the compounds, but that one of the 10,000 rats did develop mild symptoms. Such a result would be considered very successful by any standard. Such a result, however,

would actually constitute evidence of "failure" insofar as prevention is concerned. It is suggested that the term "preventing" be deleted from claims 1 and 5.

Claims 16-30 and 32-34 are also rejected under 35 USC §112 first paragraph. Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-30 and 32-34 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have shown that copolymer-1 can be used to treat GVDH. However, copolymer-1 is excluded from the claims. Thus, none of the compounds within the claimed genus has been tested in any assay. One cannot extrapolate from results with COP-1 to other random polymers. Minor structural alterations can eliminate activity; "undue experimentation" would be required to determine which copolymers will be

effective.

✧

Claims 19, 20, 25, 27, 29, 34 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of the cited claims recites the term "about" in reference to a range, thereby rendering the claims indefinite as to the upper and lower limits.

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

✧

Claim 16 is rejected under 35 U.S.C. §102(e) as being anticipated by Jameson (USP

5,958,882).

Jameson discloses various peptides that are useful to treat GVHD and transplantation rejection. Among these is SEQ ID NO:7 (see also col 19, line 37+; col 20, line 8) which has the following sequence:

Cys-Glu-Leu-Glu-Asn-Arg-Lys-Glu-Glu-Val-Glu-Trp-Val-Phe-Lys-Val-Thr-Cys

This peptide contains Glu, Arg, Trp and Lys, thereby meeting the amino acid composition requirements.

The instant claims recite the term "random copolymer". However, a practitioner of the claimed invention has to first decide on an amino acid composition; in this respect the copolymers (of the instant claims) are not random. As for the prior art peptide, this peptide could have been made by a random process, once a decision has been made with regard to the amino acid composition. This random process would include, e.g., polymerization of N-carboxyanhydrides, as well as combinatorial library production and screening.

Thus, the claim is anticipated.

✧

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 16 is rejected under 35 U.S.C. §103 as being unpatentable over Aharoni (USP 5,858,964).

Aharoni discloses copolymer-1 and compositions containing it.

This rejection is not imposed under 35 USC §102 because of the following phrase in claim 1:

"the random copolymer is not Cop-1... when the disease... is GVHD"

This rejection, however, is justified under §103.

First, the disclosed peptide could be used to treat host versus graft disease, rather than graft versus host disease. It would have been obvious to one of ordinary skill that a compound which is effective to treat GVDH will be effective to treat HVGD. Thus, the claims are

rendered obvious on that basis.

Second, it may be the case (or may not) that copolymer-1 is itself excluded from the claim. But what is not excluded is a peptide in which a single Lys, Arg, Glu, Ala, Tyr or Trp residue is replaced with a corresponding homolog differing by one methylene unit. For example, suppose that one had the following (so-called) "GLAT" peptide:

E-K-A-Y-Y-A-E-**K**-A-A-Y-E-K-K-A-E

Compare this with the following ("O" represents ornithine):

E-K-A-Y-Y-A-E-**O**-A-A-Y-E-K-K-A-E

A peptide biochemist of ordinary skill would have expected, *a priori*, that when a side chain of one amino acid in a peptide is extended by one methylene unit, the biological activity of that peptide will remain substantially the same [*In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544)]. The peptide that contains the ornithine is not copolymer-1, and so the proviso in claim 1 is circumvented. Thus, the claims are rendered obvious on this basis.

Thus, the claims are rendered obvious.

✧

Claims 16-17 are rejected under 35 U.S.C. §103 as being unpatentable over Leto (USP 5,182,262).

Leto discloses the following peptide at several locations:

**Lys**-Thr-**Ala**-Ser-Pro-**Trp**-**Lys**-Ser-Ala-Arg-Leu-Met-Val-His-Thr-Val-Ala-Thr-Phe-Asn-Ser-Ile-Lys-**Glu**.

Also disclosed (e.g., col 1, line 54+; col 15, line 26-27) is that the peptide can be used to treat tissue transplant rejection and tissue graft rejection. It may be true that the term "GVDH" is not used, but the immunologist of ordinary skill would expect that if a compound is effective to treat tissue transplant rejection and tissue graft rejection, it will be effective to treat GVDH.

The instant claims recite the term "random copolymer". However, a practitioner of the claimed invention has to first decide on an amino acid composition; in this respect the copolymers (of the instant claims) are not random. As for the prior art peptide, this peptide could have been made by a random process, once a decision has been made with regard to the the amino acid composition.

Thus, the claims are rendered obvious.

✧

Claim 16 is rejected under 35 U.S.C. §103 as being unpatentable over Jameson (USP 6,180,600).

Jameson discloses various peptides for treating organ transplant rejection and GVDH. Among the peptides disclosed for this purpose are SEQ ID NOS: 3, 15 and 17, each of which have the requisite amino acids.

Thus, the claims are rendered obvious.

✧

Claim 16 is rejected under 35 U.S.C. §103 as being unpatentable over Clayberger (USP 6436903)

Clayberger discloses various peptides for treating organ transplant rejection and GVDH. Among the peptides disclosed for this purpose are SEQ ID NOS: 14-22, each of which contain the requisite amino acids.

Thus, the claims are rendered obvious.

✺

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600